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FILE 'IFIPAT' ENTERED AT 17:00:45 ON 06 OCT 2002

```
=> s eugenol
L1       21715 EUGENOL

=> s methoxyestradiol
L2        2430 METHOXYESTRADIOL

=> s l1 and l1
L3       21715 L1 AND L1

=> s l1 and l2
L4          26 L1 AND L2

=> d l4 1-26 bib abs
```

L4 ANSWER 1 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:458743 BIOSIS
DN PREV200100458743
TI Development of novel apoptotic inducers for prostate cancer therapy.
AU Kumar, Addanki P. (1); Garcia, Gretchen E.; Rajnarayanan, Rajendram; Alworth, William L.; Slaga, Thomas J.
CS (1) AMC Cancer Research Center, Denver, CO USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 448. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.
DT Conference
LA English
SL English

L4 ANSWER 2 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:228282 BIOSIS
DN PREV199497241282
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li, Yunbo; Trush, Michael A. (1)
CS (1) Dep. Environ. Health Sci., Room 7032, Johns Hopkins Sch. Hygiene Public Health, 615 N. Wolfe St., Baltimore, MD 21205 USA
SO Cancer Research, (1994) Vol. 54, No. 7 SUPPL., pp. 1895S-1898S.
ISSN: 0008-5472.
DT Article
LA English
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded vphi-X-174 RF I DNA (vphi-X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tertbutylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H-2O-2 generation are tow major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 3 OF 26 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
AN 1994:24132141 BIOTECHNO
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li Y.; Trush M.A.

CS Environmental Health Sciences Dept., J. Hopkins Hygiene/Public Hlth. Sch., 615 N. Wolfe Street,Baltimore, MD 21205, United States.
SO Cancer Research, (1994), 54/7 SUPPL. (1895s-1898s)
CODEN: CNREA8 ISSN: 0008-5472
DT Journal; Conference Article
CY United States
LA English
SL English
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4- hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded .vphi.X-174 RF I DNA (.vphi.X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2- hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H.sub.2O.sub.2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound- induced DNA damage in target cells.

L4 ANSWER 4 OF 26 CANCERLIT
AN 94185039 CANCERLIT
DN 94185039 PubMed ID: 8137307
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li Y; Trush M A
CS Department of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21205.
NC ES03760 (NIEHS)
ES03819 (NIEHS)
ES05131 (NIEHS)
+
SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 94185039
EM 199404
ED Entered STN: 19941107
Last Updated on STN: 19970509
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation

of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS
AN 2002:575756 CAPLUS
DN 137:103879
TI Use of **eugenol**, alone and in combination with 2-**methoxyestradiol**, as prophylaxis for cancers
IN Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
PA USA
SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No. 527,283, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002103174	A1	20020801	US 2001-4105	20011204
	US 2002068724	A1	20020606	US 2001-777151	20010205
PRAI	US 2000-527283	B2	20000317		
	US 2001-777151	A2	20010205		
	US 2001-777559	B2	20010206		

AB The invention discloses the use of **eugenol**, alone and in combination with 2-**methoxyestradiol** in the context of prostate cancer prophylaxis and treatment, and in the treatment and prevention of noncancerous enlargement of prostate glands.

L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2002 ACS
AN 2002:221214 CAPLUS
DN 136:241655
TI Estradiol derivatives as agents and methods for the prevention of initial onset and recurrence of existing cancers
IN Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
PA Oncology Sciences Corporation, USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 527,283, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002035098	A1	20020321	US 2001-808408	20010314
	WO 2002072021	A2	20020919	WO 2002-US7445	20020313

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2000-527283	B2	20000317		
	US 2001-808408	A1	20010314		

AB The use of 2-**methoxyestradiol**, analogs of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of 2-**methoxyestradiol** and its analogs with synergistic compds. (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers is described.

L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
AN 2002:51983 CAPLUS
DN 136:79754
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
IN Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
PA Biochemix, Inc., USA
SO U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U. S. Ser. No. 527,283, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002006918	A1	20020117	US 2001-780269	20010209
	WO 2002062348	A1	20020815	WO 2002-US2826	20020201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	WO 2002062347	A1	20020815	WO 2002-US2827	20020201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	WO 2002062349	A1	20020815	WO 2002-US2828	20020201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2000-527283	B2	20000317		
	US 2001-777151	A1	20010205		
	US 2001-777559	A1	20010206		

US 2001-780269 A1 20010209
AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxis and treatment.

L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS
AN 1994:238022 CAPLUS
DN 120:238022
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Tursh, Michael A.
CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Cancer Research (1994), 54(7, Suppl.), 1895s-1898s
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely assocd. with chromosomes and DNA bases, in this study the authors have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compds. by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concns. of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compds. including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity anal. shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compds. with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compds. having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addn., the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the obsd. DNA damage. Using reactive oxygen scavengers, it was obsd. that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromol.-assocd. copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compd.-induced DNA damage in target cells.

L4 ANSWER 9 OF 26 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 2001-47952 DRUGU P
TI Development of novel apoptotic inducers for prostate cancer therapy.
AU Kumar A P; Garcia G E; Rajnarayanan R; Alworth W L; Slaga T J
CS AMC-Cancer-Res.Cent.; Univ.Tulane
LO Denver, Colo.; New Orleans, La., USA
SO Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 448, 2001) 1 Ref. ISSN: 0197-016X
AV AMC Cancer Research Center, Denver, CO, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 2001-47952 DRUGU P
AB This study elucidated 2-**methoxyestradiol**'s (2-ME) critical moiety for tumor growth growth inhibition. The effect of 16-epiestriol, **Eugenol** (4-allyl-2-methoxyphenol), curcumin, 4-methoxyphenol (mequinol) in inhibiting human prostate cancer cell growth was studied.

16-Epiestriol had no growth inhibitory activity indicating that the methoxy group was critical for its growth inhibitory activity. Conversely **eugenol** inhibited the growth of prostate cancer cells indicating those structures simpler than the steroidal nucleus can also be developed as therapeutics for prostate cancer. The IC50s for curcumin and 4-methoxyphenol was much higher than 2-ME and **eugenol**. (conference abstract: 92nd Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, USA, 2001). (No EX).

ABEX (E124)

L4 ANSWER 10 OF 26 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1994-25367 DRUGU P B E S
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li Y; Trush M A
CS Univ.Johns-Hopkins
LO Baltimore, Maryland, United States
SO Cancer Res. (54, No. 7, Suppl., 1895s-1898s, 19 1 Fig. 2 Tab. 31 Ref.
CODEN: CNREA8 ISSN: 0008-5472
AV Department of Environmental Health Sciences, Room 7032, The Johns Hopkins School of Hygiene and Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, U.S.A. (M.A.T.).
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 1994-25367 DRUGU P B E S
AB With uM levels of cupric sulfate (Fisher-Sci.), DNA strand breaks were induced by 1,4-hydroquinone (HQ), 4,4-biphenol, catechol (all Sigma-Chem.), 1,2,4-benzenetriol (Aldrich), 2-**methoxyestradiol** (Sigma-Chem.), hydroxyestradiol (Steraloids), diethylstilbestrol, butylated-hydroxytoluene (BHT), butylated-hydroxyanisole (BHA), tert-butylhydroquinone (BHQ, all Sigma-Chem.), ferulate, caffeate, chlorogenate (all Aldrich), **eugenol**, paracetamol and acetaminodophenol-2 (all Sigma-Chem.). The induced strand breaks were inhibited by bathocuproinedisulfonate (BCS). The DNA cleaving activity for compounds with a 1,4-hydroquinone structure was greater than those with a catechol group. Benzo(a)pyrene, estradiol (E2, Sigma-Chem.) and 4-hydroxy-E2 (steraloids) caused no DNA damage.
ABEX In the presence of 10 uM Cu(II), 10 uM HQ induced extensive DNA strand breaks; this effect was inhibited by BCS (40 uM). Catalase, but not Cu, Zn superoxide dismutase, inhibited the HQ/Cu(II)-induced DNA strand breaks; anaerobic conditions were also protective. Among mannitol, N-tert-butyl alpha-phenylnitrone, Na azide and 2,2,6,6-tetramethyl 4-piperidone, the hydroxyl radical scavengers did not prevent the HQ/Cu(II)-induced DNA strand breaks, whereas the single oxygen scavengers had some inhibitory effect. 1,2,4-benzenetriol was more effective than phenol, 4,4'-biphenol and catechol at causing DNA strand breaks in the presence of Cu(II). 2-Hydroxyestradiol/Cu(II) caused extensive DNA strand breaks as well as significant O2 consumption and H2O2 generation. 2-**Methoxyestradiol**/Cu(II) only induced slight DNA strand breaks, and 4-hydroxyestradiol/Cu(II) showed no DNA cleaving activity. Diethylstilbestrol/Cu(II) was only slight effective. In the presence of Cu(II), BHQ induced extensive DNA degradation, while BHA and BHT were less potent. Caffeate/Cu(II) showed a stronger DNA cleaving capability than did ferulate. In the presence of Cu(II), chlorogenate, **eugenol**, 2-acetamidophenol and paracetamol induced only slight DNA strand breaks, while benzo(a)pyrene did not damage. (E61/MB)

L4 ANSWER 11 OF 26 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 94133041 EMBASE
DN 1994133041
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li Y.; Trush M.A.
CS Environmental Health Sciences Dept., J. Hopkins Hygiene/Public Hlth. Sch.,

615 N. Wolfe Street,Baltimore, MD 21205, United States
SO Cancer Research, (1994) 54/7 SUPPL. (1895s-1898s).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Conference Article
FS 016 Cancer
LA English
SL English
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4- hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2- hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure- activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 12 OF 26 IFIPAT COPYRIGHT 2002 IFI
AN 10159532 IFIPAT;IFIUDB;IFICDB
TI USE OF **EUGENOL**, ALONE, AND IN COMBINATION WITH OTHER CHEMOPREVENTATIVE AGENTS AS PROPHYLAXIS FOR CANCERS
INF Alworth; William, New Orleans, LA, US
Kumar; Addanki P., Denver, CO, US
Slaga; Thomas J., Golden, CO, US
IN Alworth William; Kumar Addanki P; Slaga Thomas J
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
PI US 2002103174 A1 20020801
AI US 2001-4105 20011204
RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
US 2001-777151 20010205 CONTINUATION-IN-PART PENDING
US 2001-777559 20010206 CONTINUATION-IN-PART ABANDONED
FI US 2002103174 20020801
DT Utility; Patent Application - First Publication
FS CHEMICAL
FS APPLICATION
CLMN 9
AB The use of **eugenol**, alone and in combination with 2methoxyestradiol (2-ME) in the context of prostate cancer prophylaxes and treatment, and in the treatment and prevention of non-cancerous enlargement of prostate glands.
CLMN 9

L4 ANSWER 13 OF 26 IFIPAT COPYRIGHT 2002 IFI
AN 10091534 IFIPAT;IFIUDB;IFICDB
TI AGENTS AND METHODS FOR THE PREVENTION OF INITIAL ONSET AND RECURRENCE OF EXISTING CANCERS
INF Alworth; William, New Orleans, LA, US
Kumar; Addanki P., Denver, CO, US
Slaga; Thomas J., Denver, CO, US
IN Alworth William; Kumar Addanki P; Slaga Thomas J
PAF Oncology Sciences Corporation, Austin, TX, US
PA Oncology Sciences Corp
AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
PI US 2002035098 A1 20020321
AI US 2001-808408 20010314
RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
FI US 2002035098 20020321
DT Utility; Patent Application - First Publication
FS CHEMICAL
FS APPLICATION
CLMN 15
AB The use of 2-**methoxyestradiol**, analogues of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of the 2 **methoxyestradiol** and its analogues with synergistic compounds (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers.
CLMN 15

L4 ANSWER 14 OF 26 IFIPAT COPYRIGHT 2002 IFI
AN 10063396 IFIPAT;IFIUDB;IFICDB
TI USE OF **EUGENOL**, ALONE, AND IN COMBINATION WITH OTHER CHEMOPREVENTATIVE AGENTS AS PROPHYLAXIS FOR CANCERS; PROSTATE CANCER
INF Alworth; William, New Orleans, LA, US
Kumar; Addanki P., Denver, CO, US
Slaga; Thomas J., Austin, TX, US
IN Alworth William; Kumar Addanki P; Slaga Thomas J
PAF Biochemix, Inc., Austin, TX, US
PA Biochemix Inc
AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
PI US 2002006918 A1 20020117
AI US 2001-780269 20010209
RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
FI US 2002006918 20020117
DT Utility; Patent Application - First Publication
FS CHEMICAL
FS APPLICATION
CLMN 5
AB The use of **eugenol**, alone and in combination with 2methoxyestradiol (2-ME) in the context of prostate cancer prophylaxes and treatment.
CLMN 5

L4 ANSWER 15 OF 26 LIFESCI COPYRIGHT 2002 CSA
AN 95:3046 LIFESCI
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Trush, M.A.*
CS Dep. Environ. Health Sci., Rm. 7032, Johns Hopkins Sch. Hyg. and Pub. Health, 615 N. Wolfe St., Baltimore, MD 21205, USA
SO CANCER RES., (1994) vol. 54, no. 7 suppl., pp. 1895S-1899S.
ISSN: 0008-5472.
DT Journal
FS N
LA English
SL English
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since

copper exists in the nucleus and is closely associated with chromosomes and DNA bases, we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded Phi X-174 RF I DNA (Phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H sub(2)O sub(2) generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 16 OF 26 MEDLINE
AN 94185039 MEDLINE
DN 94185039 PubMed ID: 8137307
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li Y; Trush M A
CS Department of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21205.
NC ES03760 (NIEHS)
ES03819 (NIEHS)
ES05131 (NIEHS)
+
SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
ED Entered STN: 19940509
Last Updated on STN: 19970203
Entered Medline: 19940425
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity

for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 17 OF 26 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 94:195003 SCISEARCH
GA The Genuine Article (R) Number: NE168
TI REACTIVE OXYGEN-DEPENDENT DNA-DAMAGE RESULTING FROM THE OXIDATION OF PHENOLIC-COMPOUNDS BY A COPPER-REDOX CYCLE MECHANISM
AU LI Y B (Reprint); TRUSH M A
CS JOHNS HOPKINS UNIV, SCH HYG & PUBL HLTH, DEPT ENVIRONM HLTH SCI, DIV TOXICOL SCI, ROOM 7032, BALTIMORE, MD, 21205 (Reprint)
CYA USA
SO CANCER RESEARCH, (01 APR 1994) Vol. 54, No. 7, Supp. S, pp. S1895-S1898. ISSN: 0008-5472.
DT Article; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phiX-174 RF I DNA (phiX-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 18 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 2002:182446 TOXCENTER
CP Copyright 2002 ACS
DN CA13708103879V
TI Use of **eugenol**, alone and in combination with 2-**methoxyestradiol**, as prophylaxis for cancers
AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
PI US 2002103174 A1 1 Aug 2002
SO (2002) U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No. 527,283, abandoned.
CODEN: USXXCO.
CY UNITED STATES
DT Patent
FS CAPLUS
OS CAPLUS 2002:575756
LA English
ED Entered STN: 20020820
Last Updated on STN: 20020820
AB The invention discloses the use of **eugenol**, alone and in combination with 2-**methoxyestradiol** in the context of prostate cancer prophylaxis and treatment, and in the treatment and prevention of noncancerous enlargement of prostate glands.

L4 ANSWER 19 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 2002:84120 TOXCENTER
CP Copyright 2002 ACS
DN CA13616241655Z
TI Estradiol derivatives as agents and methods for the prevention of initial onset and recurrence of existing cancers
AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
CS ASSIGNEE: Oncology Sciences Corporation
PI US 2002035098 A1 21 Mar 2002
SO (2002) U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 527,283, abandoned.
CODEN: USXXCO.
CY UNITED STATES
DT Patent
FS CAPLUS
OS CAPLUS 2002:221214
LA English
ED Entered STN: 20020409
Last Updated on STN: 20020423
AB The use of 2-**methoxyestradiol**, analogs of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of 2-**methoxyestradiol** and its analogs with synergistic compds. (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers is described.

L4 ANSWER 20 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 2002:36024 TOXCENTER
CP Copyright 2002 ACS
DN CA13606079754G
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
CS ASSIGNEE: Biochemix, Inc.
PI US 2002006918 A1 17 Jan 2002
SO (2002) U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U. S. Ser. No. 527,283, abandoned.
CODEN: USXXCO.
CY UNITED STATES
DT Patent
FS CAPLUS
OS CAPLUS 2002:51983
LA English

ED Entered STN: 20020205
Last Updated on STN: 20020423
AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxis and treatment.

L4 ANSWER 21 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:140310 TOXCENTER
CP Copyright 2002 ACS
DN CA12019238022E
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Tursh, Michael A.
CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA.
SO Cancer Research, (1994) Vol. 54, No. 7, Suppl., pp. 1895s-1898s.
CODEN: CNREA8. ISSN: 0008-5472.
CY UNITED STATES
DT Journal
FS CAPLUS
OS CAPLUS 1994:238022
LA English
ED Entered STN: 20011116
Last Updated on STN: 20020917
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely assocd. with chromosomes and DNA bases, in this study the authors have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compds. by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concns. of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compds. including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity anal. shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compds. with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compds. having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addn., the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the obsd. DNA damage. Using reactive oxygen scavengers, it was obsd. that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromol.-assocd. copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compd.-induced DNA damage in target cells.

L4 ANSWER 22 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:81496 TOXCENTER
CP Copyright 2002 BIOSIS
DN PREV199497241282
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Trush, Michael A. (1)
CS (1) Dep. Environ. Health Sci., Room 7032, Johns Hopkins Sch. Hygiene Public Health, 615 N. Wolfe St., Baltimore, MD 21205 USA
SO Cancer Research, (1994) Vol. 54, No. 7 SUPPL., pp. 1895S-1898S.
ISSN: 0008-5472.

DT Article
FS BIOSIS
OS BIOSIS 1994:228282
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded vphi-X-174 RF I DNA (vphi-X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tertbutylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H-2O-2 generation are tow major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 23 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:31261 TOXCENTER
DN 94185039 PubMed ID: 8137307
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li Y; Trush M A
CS Department of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21205
NC ES03760 (NIEHS)
ES03819 (NIEHS)
ES05131 (NIEHS)
+
SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.
Journal Code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDLINE
OS MEDLINE 94185039
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116
AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar

concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 24 OF 26 USPATFULL
AN 2002:192103 USPATFULL
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
IN Slaga, Thomas J., Golden, CO, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PI US 2002103174 A1 20020801
AI US 2001-4105 A1 20011204 (10)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED Continuation-in-part of Ser. No. US 2001-777151, filed on 5 Feb 2001, PENDING Continuation-in-part of Ser. No. US 2001-777559, filed on 6 Feb 2001, ABANDONED
DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 287
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxes and treatment, and in the treatment and prevention of non-cancerous enlargement of prostate glands.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 25 OF 26 USPATFULL
AN 2002:61262 USPATFULL
TI Agents and methods for the prevention of initial onset and recurrence of existing cancers
IN Slaga, Thomas J., Denver, CO, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PA Oncology Sciences Corporation, Austin, TX, UNITED STATES (U.S. corporation)
PI US 2002035098 A1 20020321
AI US 2001-808408 A1 20010314 (9)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED

DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of 2-**methoxyestradiol**, analogues of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of the 2 **methoxyestradiol** and its analogues with synergistic compounds (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 26 OF 26 USPATFULL
AN 2002:12537 USPATFULL
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
IN Slaga, Thomas J., Austin, TX, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PA Biochemix, Inc., Austin, TX, UNITED STATES (U.S. corporation)
PI US 2002006918 A1 20020117
AI US 2001-780269 A1 20010209 (9)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED
DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 175
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxes and treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

PI WO 9640150 A1 19 Dec 1996
SO (1996) PCT Int. Appl., 31 pp.
CODEN: PIXXD2.
CY UNITED STATES
DT Patent
FS CAPLUS
OS CAPLUS 1997:127459
LA English
ED Entered STN: 20011116
Last Updated on STN: 20020626
AB A method for treating and preventing **benign prostatic hyperplasia** (BPH) and prostatic carcinoma involves administering a therapeutically effective amt. of a compd. which binds to SHBG and antagonizes the SHBG-mediated effects of both estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol by preventing the binding of estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol. Also disclosed are the compds. which bind SHBG and prevent the binding of estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol, as well as a method of finding compds. which bind to SHBG and prevent the binding of estradiol.
TI Treatment and prevention of prostatic disease, including prostate cancer and **benign prostatic hyperplasia**, with compounds binding to sex hormone-binding globulin (SHBG), and method for therapeutic compound identification
AB A method for treating and preventing **benign prostatic hyperplasia** (BPH) and prostatic carcinoma involves administering a therapeutically effective amt. of a compd. which binds to SHBG and antagonizes the. . .
ST Miscellaneous Descriptors
sex hormone binding globulin antagonist therapeutic; **benign prostatic hyperplasia** SHBG antagonist; prostate disease SHBG antagonist; cancer prostate SHBG antagonist
RN . . . (Flutamide)
19216-56-9 (Prazosin)
63590-64-7 (Terazosin)
74191-85-8 (Doxazosin)
90357-06-5 (Casodex)
106133-20-4 (Tamsulosin)
119169-78-7 (Epristeride)
521-17-5 (.DELTA.5-Androstene-3.beta.,17.beta.-diol)
6038-31-9 (5.beta.-Androstan-3.beta.,17.beta.-diol)
58-22-0 (Testosterone)
362-07-2 (**2-Methoxyestradiol**)
521-18-6 (Dihydrotestosterone)
60-92-4 (Cyclic AMP)
RN 1852-53-5; 81403-80-7; 98319-26-7; 158493-17-5; 166174-54-5; 166174-94-3; 186446-10-6; 1851-23-6; 571-20-0; 16895-59-3

The Genuine Article (R) Number: YN232

TI Sex hormone-binding globulin mediates prostate androgen receptor action via a novel signaling pathway

AU Ding V D H (Reprint); Moller D E; Feeney W P; Didolkar V; Nakhla A M; Rhodes L; Rosner W; Smith R G

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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Estradiol (E-2) and 5 alpha-androstan-3 alpha,17 beta-diol (3 alpha-diol) have been implicated in prostate hyperplasia in man and dogs, but neither of these steroids bind to androgen receptors (ARs). Recently, we reported that E-2 and 3 alpha-diol stimulated generation of intracellular cAMP via binding to a complex of sex hormone-binding globulin (SHBG) and its receptor (R-SHBG) On prostate cells. We speculated that this pathway, involving steroids normally found in the prostate, was involved in the indirect activation of ARs. Using the dog as a model to test this hypothesis in normal prostate, we investigated whether E-2, 3 alpha-diol, and SHBG stimulated the production of the androgen-responsive protein, arginine esterase (AE), the canine equivalent of human prostate-specific antigen. In cultured dog prostate tissue preincubated with SHBG, E-2 and 3 alpha-diol stimulated AE activity. These effects were blocked by hydroxyflutamide, an AR antagonist, and by **2-methoxyestradiol**, a competitive inhibitor of E-2 and 3 alpha-diol binding to SHBG. In the absence of exogenous steroids and SHBG, AE also was significantly increased by treatment with forskolin or 8-Bromaodenosine-cAMP. These observations support the hypothesis that in normal prostate, E-2 and 3 alpha-diol can amplify or substitute for androgens, with regard to activation of the AR via the R-SHBG by a signal transduction pathway involving cAMP. Because both E-2 and 3 alpha-diol are involved in the pathogenesis of **benign prostatic hyperplasia** in dogs and implicated in **benign prostatic hyperplasia** in man, antagonism of the prostatic SHBG pathway may offer a novel and attractive therapeutic target.

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TI Treatment and prevention of prostatic disease, including prostate cancer and **benign prostatic hyperplasia**, with compounds binding to sex hormone-binding globulin (SHBG), and method for therapeutic compound identification

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